Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendments, claims 1, 3-10, 13, and 25-50 are pending in the application, with 1, 8, 9, 10, 31, 38 and 44 being the independent claims. Claim 13 is allowed. Claim 24 has been cancelled. New claims 38-50 have been added. Support for the amendment to claims 1 and 31 can be found, *inter alia*, at page 63-66, Figures 7A-D, Figure 8 and page 34, line 24, through page 35, line 10, of the specification. Support for the amendments to claims 8-10 can be found, *inter alia*, at page 21, lines 7-25, of the specification. Support for new claims 38-50 can be found, *inter alia*, at page 17, lines 13-24, of the specification. No new matter has been introduced by these amendments.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Examiner Interview

The Applicants thank Examiner Harris for the courtesy extended to their representatives in a telephonic interview on August 17, 2004. The Examiner's Interview Summary accurately reflects the substance of the interview, and should be made of record.

Priority

In the Office Action, pages 3-4, the Examiner contends that Applicants have not supplied corroborative evidence that establishes that resequenced SEQ ID NOS:1-3 are in fact one in the same as the deposited clones and that of the priority documents. In an abundance of caution, Applicants have withdrawn samples of the three biological deposits (ATCC Deposit Nos. 209933, 209934 and 98809) and are still in the process of resequencing the clones. Unfortunately, until that task has been completed, Applicants are unable to submit a Declaration under 37 C.F.R. § 1.132 by an inventor at this time in order to substantiate that the deposited sequences are the same as the corrected sequences, submitted on July 23, 2001. Applicants will submit the Declaration as soon as possible.

Objections to the Specification

The Examiner objected to Figures 1A, 1B-1, 1C, 2A, 2B, 2C, 3A and 3B under 35 U.S.C. § 132 as allegedly introducing new matter into the disclosure. The Examiner objected to the Figures as introducing new matter in view of the Applicants' amendments to the Figures to bring them into conformity with the amended sequence listing. As stated above, Applicants have withdrawn samples of the three biological deposits (ATCC Deposit Nos. 209933, 209934 and 98809) and are still in the process of resequencing the clones. Unfortunately, until that task has been completed, Applicants are unable to submit a Declaration under 37 C.F.R. § 1.132 by an inventor at this time in order to substantiate that the deposited sequences are the same as

the corrected sequences, submitted on July 23, 2001. Accordingly, Applicants respectfully request that the Examiner hold this objection in abeyance.

Rejections Under 35 U.S.C. § 112, First Paragraph (written description)

The Examiner rejected claims 8 and 10 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. *Office Action* at pp. 4-5. Applicants respectfully traverse this written description/new matter rejection.

Briefly, the Examiner's position is that the disclosure cited by Applicants (page 21, lines 17-25 of the specification) does not support the "unambiguous contemplation of at least 50 and 100 nucleotides." The Examiner further argues that the disclosure "does not support the exclusion of polynucleotides less than 50 nucleotides and 100 nucleotides" for claims 8 and 10, respectively. *Id.* at p. 5.

An Applicant satisfies the written description requirement when the disclosure of the application relied upon conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. See *e.g.*, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-1564. How the specification accomplishes this goal is not material. *In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976). The invention claimed does not have to be described in *ipsis verbis* in the specification in order to satisfy the description requirement but must be supported through express, implicit, or inherent disclosure. *See* MPEP § 2163. Further, the burden of showing that the claimed invention is not described in the specification rests on the Patent and

Trademark Office in the first instance, and it is up to the PTO to give reasons why a description not in *ipsis verbis* is insufficient. 541 F.2d at 265.

At the outset, Applicants respectfully submit that the specification expressly discloses polynucleotide fragments of at least 50 nucleotides of SEQ ID NO:1 as claimed in claim 8. The Applicants respectfully direct the Examiner's attention to page 25 of the specification:

> Polynucleotides of the invention which are sufficiently identical to a nucleotide sequences contained in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 or SEQ ID NO:4, or in the cDNA inserts of ATCC Deposit No. 209933, ATCC Deposit No. 209934, ATCC Deposit No. 98809 or ATCC Deposit No. 326637, may be used as hybridization probes for cDNA and genomic DNA, to isolate full-length cDNAs and genomic clones encoding *de novo* DNA cytosine methyltransferase proteins and to isolate cDNA and genomic clones of other genes that have a high sequence similarity to the *de novo* DNA cytosine methyltransferase genes. Such hybridization techniques are known to those of skill in the art. Typically, these nucleotide sequences are at least about 90% identical, preferably at least about 95% identical, more preferably at least about 97%, 98% or 99% identical to that of the reference. The probes generally will comprise at least 15 nucleotides. Preferably, such probes will have at least 30 nucleotides and may have *at least 50 nucleotides*. Particularly preferred probes will range between 30 and 50 nucleotides.

Specification at p. 25, lines 15-29 (emphasis added).

While the specification does not in *ipsis verbis* recite fragments of SEQ ID NO:3 containing at least 100 nucleotides, the Applicants maintain that the specification implicitly discloses that Applicants contemplated fragments of at least 100 nucleotides in length. The Applicants chose to describe the fragment lengths in the following way:

> Generally, polynucleotide fragments of the invention may be defined algebraically in the following way: (a) for SEQ

> ID NO:1, as 15 + N, wherein N equals zero or any positive integer up to 4176; (b) for SEQ ID NO:2, as 15 + N, wherein N equals zero or any positive integer up to 4180; and (c) for SEQ ID NO:3, as 15 + N, wherein N equals zero or any positive integer up to 4401.

Specification, p. 21, lines 17-25. In this case, the Applicants chose to describe the fragment lengths by formula, rather than individually listing each fragment size. If the Applicant were required to in *ipsis verbis* recite each individual fragment size, as the Examiner seems to require, then Applicants would be required to recite more than 12,000 individual fragment sizes in the specification in order to obtain claims to all fragments of SEQ ID NOS:1, 2, and 3. This would pose an unreasonable and restrictive burden on the Applicants and would not convey any additional information to one skilled in the art. The courts have emphatically rejected such rigid rules deciding instead that is immaterial *how* the Applicant satisfies the disclosure requirement. *See, e.g., Lockwood v. American Airlines*, Inc. 107 F.3d 1565, 1572 (Fed Cir. 1997)("written description" requirement may be satisfied by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). *See also Vas-Cath*, 935 F.2d at 1565 ("drawings alone may provide a 'written description' of an invention as required by Sec. 112\"); *Autogiro Co. of America v. United States*, 384 F.2d 391, 398 (Ct. Cl. 1967)("In those instances where a visual representation can flesh out words, drawings may be used in the same manner and with the same limitations as the specification."); *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997)("In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the

claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.").

Further, the Applicants respectfully submit that the Examiner has not met the initial burden of presenting evidence or reasoning to explain why a person of ordinary skill in the art would not recognize in the disclosure a description of the invention defined by the claims. The Applicants respectfully submit the Examiner's argument that the disclosure "does not support the exclusion of polynucleotides less than 50 nucleotides and 100 nucleotides for claims 8 and 10, respectively" is not a valid basis to support the rejection. The Federal Circuit in *Vas-Cath* rejected such a legal standard applied by a lower court. The court stated, "[t]he court further erred in applying a legal standard that essentially required the drawings of the '081 design application to necessarily *exclude* all diameters other than those within the claimed range." 935 F.2d at 1566 (emphasis added). The court in *Wertheim* similarly stated "[t]hat what appellants claim as patentable to them is less than what they described as their invention is not conclusive if their specification also reasonably describes that which they do claim." 541 F.2d at 263.

The facts in *Wertheim* are analogous to the facts in this case. In *Wertheim*, the appellants disclosed a process for concentrating and freeze drying coffee that required preparing an extract with a solids content "between 25% and 60%." *Id.* at 259. The appellants later amended their claims in a later application to recite "between 35% and 60%," although the specification did not recite this limitation in *ipsis verbis*. *Id.* at 264. The issue in *Wertheim* was whether the PTO has presented sufficient reason to doubt that the broader described range also described the somewhat narrower claimed range. *Id.*

The court stated that where it is clear, for instance, that the broad described range pertains to a different invention than the narrower (and subsumed) claimed range, the broader range does not describe the narrower range. *Id.* at 265. Applying this rule, the court held that the description requirement was met because persons skilled in the art would consider processes employing a 35% - 60% solids content range to be part of appellant's invention and that the PTO did not make any distinction, in terms of the operability of the process or of achieving any desired result between the claimed lower limits of solids content (35% - 60%) and that disclosed in the application (25% - 60%). *Id.*

Applicants' specification describes fragments of 15-4191 and 15-4416 nucleotides for SEQ ID NOS:1 and 3, respectively, and Applicants originally claimed nucleotides comprising at least 20 nucleotides of SEQ ID NOS:1 and 3. Applicants subsequently amended their claims to cover part of what was originally described. Like *Wertheim*, Applicants respectfully submit the Examiner has not made any distinction in terms of achieving any desired result between the range of polynucleotide fragments originally claimed and disclosed in the specification and the claimed range of polynucleotide fragments. One skilled in the art would recognize the disclosed range and claimed range of fragments have some similar applications, *e.g.*, as probes to screen for Dnmt3 expression. Consequently, one skilled in the art would conclude that, like the range of solids described in *Wertheim*, there is no difference in terms of achieving any desired result between the claimed range of polynucleotide fragments and the range of polynucleotide fragments disclosed in the specification. Moreover, the Applicants' claimed range, unlike the claimed range in *Wertheim*, is disclosed (by formula) in the

specification. Thus, the Applicants' specification more strongly supports the claimed range than that which the court found allowable in *Wertheim*.

Based on the forgoing, Applicants respectfully request that the Examiner reconsider and withdraw the written description rejection of claims 8 and 10 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 112, First Paragraph (enablement)

The Examiner rejected claims 1, 3-10, and 24-37 under 35 U.S.C. §112, first paragraph, allegedly because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention. *Office Action* at pp. 5-6. Briefly, the Examiner contends that "Applicants have not supplied information relative to the use of these claimed mutants." *Office Action*, at p. 6.

While Applicants respectfully traverse this ground of rejection as it may be applied to the pending claims, solely to advance prosecution and not in acquiescence of the Examiner's rejection, Applicants have amended claims 1 and 31 to recite that the polynucleotides encode polypeptides that are capable of methylating DNA in an *in vitro* assay.

In Example 4 (pages 63-66 of the specification) a method for screening proteins for DNA cytosine methyltransferase activity is provided. Therefore, one skilled in the art is taught how to use the claimed polynucleotides.

With respect to the claimed polynucleotide fragments of claims 8-10, Applicants maintain that the claim does not require the fragments to encode proteins or peptides that have the ability to methylate DNA. The specification discloses that the DNA fragments

may be useful as probes or primers for screening or amplifying Dnmt3 (page 21, lines 11-12; page 25, lines 15-29 of the specification). Polynucleotide fragments may also be useful for making oligonucleotides to inhibit Dnmt3 expression. *Id.* at pp. 41-52. Therefore, it is improper for the Examiner to reject claims 8-10 solely on the basis that the nucleotide fragments may not encode functional polypeptides.

Based on the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102

First, the Examiner rejected claims 1, 3, 4, 8, 9, 24-26, 29-33, 36, and 37 under 35 U.S.C. § 102(b) as allegedly anticipated by Okano *et al.* as evidenced by Accession numbers AF068625, AF068626 and AF068627. *Office Action* at p. 6. Second, the Examiner rejected claims 1, 3, 4, 8, 10, 24, 27-31, and 34-37 under 35 U.S.C. 102(b) as allegedly anticipated by Xie *et al.* as evidenced by Accession number AF067972. *Id.* at p. 7. Applicants traverse these rejections as they may be applied to the pending claims.

At the outset, Applicants respectfully point out to the Examiner that claims 31-37 are directed to, *inter alia*, polynucleotides encoding polypeptides contained in ATCC Deposit Nos. 209933, 209934, 98809, and 326637. Nowhere in these claims is the sequence identifier (SEQ ID NO) recited. Thus, even if the Applicants' effective filing date for the revised SEQ ID NOS:1, 2 and 3 is July 13, 2001, which Applicants do not concede for the reasons stated above under "***Priority***," it does not follow that Okano *et al.* and Xie *et al.* are prior art under 35 U.S.C. §102(b) to claims 31-37.

Similarly, Applicants also object to the Examiner's rejection of claim 28, which is directed to an isolated nucleic acid molecule encoding a polypeptide comprising amino acids from about 1-853 in SEQ ID NO:8. Applicants respectfully point out to the Examiner that the polynucleotide encoding SEQ ID NO:8 (*i.e.*, SEQ ID NO:4) has not been amended. Thus, it cannot be disputed that SEQ ID NO:4 is entitled to its earliest priority date.

To attest and substantiate that the deposited clones are the same as those disclosed in the PCT and provisional applications, the Examiner suggested submission of a corroborative affidavit or declaration. In an abundance of caution, Applicants have withdrawn samples of the three biological deposits (ATCC Deposit Nos. 209933, 209934 and 98809) and are still in the process of resequencing the clones. Unfortunately, until that task has been completed, Applicants are unable to submit a Declaration under 37 C.F.R. § 1.132 by an inventor at this time in order to substantiate that the deposited sequences are the same as corrected sequences, submitted on July 23, 2001. Applicants will submit the Declaration as soon as possible.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 102 or hold the rejection in abeyance until Applicants submit the Declaration.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1, 3-10, 24-26, 29-33, 36 and 37 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Okano *et al.*, as evidenced by Accession number AF068625, and Xie *et al.*, as evidenced by Accession number AF067972, in

view of Ausubel *et al.* *Office Action*, pages 7-8. Applicants respectfully traverse this ground of rejection.

To attest and substantiate that the deposited clones are the same as those disclosed in the PCT and provisional applications, the Examiner suggested submission of a corroborative affidavit or declaration. In an abundance of caution, Applicants have withdrawn samples of the three biological deposits (ATCC Deposit Nos. 209933, 209934 and 98809) and are still in the process of resequencing the clones. Unfortunately, until that task has been completed, Applicants are unable to submit a Declaration under 37 C.F.R. § 1.132 by an inventor at this time in order to substantiate that the deposited sequences are the same as corrected sequences, submitted on July 23, 2001. Applicants will submit the Declaration as soon as possible.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 103 or hold the rejection in abeyance until Applicants submit the Declaration.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202)772-8637.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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